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REMARKS/ARGUMENTS

Applicants file herewith a Request for Continued Examination and submit this paper as the submission required under 37 C.F.R. § 1.114.

Applicants have fully considered the comments the Examiner presented in an Advisory Action mailed on June 8, 2006 and respectfully request reconsideration of claims 23-70.

In the Advisory Action, the Examiner entered an Amendment filed on March 31, 2006 along with the declaration of Michael Keller, Ph.D. The Examiner also maintained a rejection of claims 23-70 under 35 USC § 112, first paragraph as not complying with the enablement requirement. In maintaining the rejection, the Examiner reiterated arguments previously made, which emphasize that the state of the art for gene therapy is unpredictable due to poor delivery efficiency provided by current vectors. (See Advisory Action, pages 2 - 4). The Examiner also responded to Applicants' arguments presented in a Response After Final that was mailed on March 31, 2006. In particular, the Examiner argued that the documents submitted and the Declaration by Dr. Keller did not demonstrate treating a genetic condition or disorder by administering the claimed compounds.

Applicants submit that the specification as originally filed and the supporting documents provided in the March 31, 2006 response provide evidence that is reasonably predictive that the claim methods are effective for treating a genetic disorder or condition in a patient. The rejection is still based on the supposed unpredictable state of the art regarding vectors as delivery systems. (Advisory Action, pages 2-4). The specification and references cited, however, suggest otherwise. The specification indicates that non-viral transfer systems using cationic liposomes are known and that the efficacy of cationic liposomes has been illustrated both *in vitro* and *in vivo* (Specification, page 1, lines 24-30). Dorin states that an attraction of gene therapy "is that symptoms can be expected to be ameliorated despite an incomplete understanding of disease pathogenesis." Id., at 799. (Gene Therapy (1996) 3, 797-801, 799).

The application and references cited in the March 31, 2006 response also show that the claims are enabled. The application provides numerous examples of *in vitro* and *in vivo* gene delivery assay studies. The *in vivo* assays measured gene delivery activity as a function of chloramphenicol acetyl transferase (CAT) activity or expression. The Alton et al. article discloses that evaluating CAT expression is a suitable way to evaluate therapeutic potential. Further, the Dorin et al. article does not merely

demonstrate that a relationship between Cftr gene expression, chloride ion transport, and survival is non linear. Rather, Dorin demonstrates that only small amounts of gene expression are necessary to provide a therapeutic effect. (Gene Therapy (1996) 3, 797-801, Abstract). Specifically, Dorin discloses that "50% of the normal level of gene expression is sufficient to prevent disease" (Abstract) and that production of 0.5 to 6% of the normal level of enzyme activity was sufficient to result in complete disappearance of lysosomal storage lesions in the liver and spleen of mutant mice. Id. at 800. That is, Dorin demonstrates that small amounts of gene expression are sufficient to treat a disorder.

Further, Dorin states that this observation may be generally applied to treating recessive diseases. Specifically, Dorin notes that "[a]lthough no correlation was made in the report between the level of enzyme and phenotype we believe that the finding supports the expectations of control analysis and underlines their generality." Id. Additionally, the nonlinear relationship between phenotype and gene activity observed for cystic fibrosis "is relevant to all recessive diseases and implies that successful gene therapy will require only partial gene correction." Id.

Thus, the evidence shows that therapeutic potential can be measured using CAT expression. The specification and Dr. Keller's declaration demonstrate that the current compounds are suitable for delivering genes to cells, as evidenced by evaluating CAT expression. Additionally, as indicated by Dorin, expressing even a small amount of enzyme or gene is suitable for providing a therapeutic (treatment) effect. Thus, given the knowledge of a person skilled in the art at the time the specification was filed, the specification enables a person skilled in the art to treat a genetic disorder by delivering a nucleic acid or nucleotide sequence to a cell using the compounds described in the claims. Consequently, Applicants submit that the specification enables a person skilled in the art to practice the claimed invention.

In addition to reconsidering claims 23-70, Applicants also add new claims 71-75 to the application. New claim 71 is directed to a method for delivering a therapeutic agent to one or more cells that comprises administering an effective amount of a composition comprising: (i) a compound comprising a cholesterol group or derivative thereof having linked thereto a head group; wherein the head group is more positive than the head group of DC-Chol; further wherein the head group is a straight chain polyamine; further wherein two or more of the amine groups of the polyamine group are separated by an ethylene group; and (ii) a nucleic acid.

Applicants respectfully request continued examination of the present application.

Respectfully submitted,

FAY, SHARPE, FAGAN,
MINNICH & McKEE, LLP

Date: 9/28/06

Scott A. McCollister, Esq., Reg. No. 33,961
Scott M. Slaby, Esq., Reg. No. 53,603
1100 Superior Avenue, Seventh Floor
Cleveland, OH 44114-2579
Telephone: 216/861-5582

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Date: September 28, 2006	Name: Laurie A. Boylan

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